Surgical results: A justification of the surgeon selection process for the ACAS trial

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Purpose: The selection of surgeons to participate in a prospective randomized trial comparing the efficacy of a surgical method with medical management is critically important because it will have a direct impact on the outcome of the study and the future use of the operation. We report the success of the method used for selecting surgeons who participated in the Asymptomatic Carotid Atherosclerosis Study (ACAS) by examining the surgical morbidity and mortality rates and the outcome of the study.
Methods: A Surgical Management Committee established criteria for auditing surgeons who wished to participate in the study. The parameters included a minimum performance of at least 12 carotid endarterectomies (CEA) per year and an audit of each surgeon's last 50 consecutive CEAs with required documentation of a combined neurologic morbidity and mortality rate of $<3.0\%$ for asymptomatic patients and $<5.0\%$ for all indications including symptomatic patients.
Results: As of February 1991, 164 surgeons from 48 medical centers applied for ACAS participation. One hundred seventeen were approved, and their aggregate experience of 5641 operations yielded a combined neurologic morbidity and mortality rate of 2.3% for asymptomatic and symptomatic patients combined. The morbidity and mortality rate for CEA on asymptomatic patients was 1.7%. These surgeons, plus those recruited after February 1991, became investigators in the ACAS trial and were responsible for the surgical care of 825 patients who were randomized to the surgical arm. Seven hundred twenty-four patients actually underwent CEA. One patient (0.14%) died and ten patients (1.38%) had strokes within the 30-day perioperative interval, for a combined stroke or death incidence of 1.52%. The 5-year stroke event rate in the surgical group (including perioperative morbidity and mortality rates) was 5.1%, compared with 11% of patients treated medically, yielding a relative risk reduction of 53% in favor of surgery ($p = 0.004$).
Conclusions: A method for selecting surgeons for participation in the ACAS trial was successful in providing low perioperative morbidity and mortality rates. This materially influenced the outcome of the study in favor of CEA. (J VASC SURG 1996;23:323-8.)

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The Asymptomatic Carotid Atherosclerosis Study (ACAS) was brought to an early conclusion on September 14, 1994, with the issuance of a clinical advisory by the National Institutes of Health that stated that a significant boundary had been crossed in favor of carotid endarterectomy (CEA). Asymptomatic patients with hemodynamically significant carotid stenoses with $>60\%$ diameter reduction had fewer strokes when treated with the combination of CEA and best medical management (325 mg aspirin and risk-factor control) than those treated with best medical management alone.[1,2]

In large part this benefit for CEA was made

possible by the low morbidity and mortality rates accomplished by ACAS-approved surgeons. The objective of this report is to describe the method by which these surgeons were selected and to determine whether the study results justify the methods for surgeon selection.

MATERIALS AND METHODS

ACAS trial design. The ACAS trial asked the following question: Among patients with severe but asymptomatic carotid stenoses, does CEA plus medical management and risk-factor control reduce the overall 5-year risk of fatal and nonfatal ipsilateral cerebral events when compared with a similar group of patients who are managed only medically?

Patients with hemodynamically significant carotid stenosis determined to be equivalent to a 60% diameter–reducing lesion of the internal carotid artery were randomly allocated to a surgical or medical arm. The design and conduct of the trial have been previously described.[2,3] Primary endpoints were any stroke or death after randomization and within the 30-day perioperative period for patients receiving CEA, a comparable 42-day period after randomization for those not assigned to surgery, and any ipsilateral stroke or stroke-related death that occurred during follow-up. Surgically treated patients were examined by the neurologist or study coordinator 24 hours after surgery to determine whether a persistent neurologic deficit was present. Patients were examined again 30 days after surgery, or 42 days after randomization in the medical group, to determine whether a neurologic deficit had occurred within that interval. All potential endpoints were reviewed by the cerebrovascular endpoints committee.

Patients with hemodynamically significant stenoses could be identified in one of three ways: (1) conventional or arterial digital subtraction angiography documenting a $\geq 60\%$ diameter–reducing lesion, as measured by comparing the minimal residual lumen with a normal distal internal carotid artery lumen in the equation $1 - (\text{MRL/DL}) \times 100$; (2) Doppler ultrasonography documenting a peak-systolic frequency or end-diastolic frequency greater than a machine-specific cutoff point with a predicted false-positive rate of $< 5.0\%$, as determined by previous correlation of Doppler flow velocities with arteriography in 50 consecutive cases; (3) Doppler ultrasonography documenting a peak-systolic frequency or end-diastolic frequency greater than a machine-specific cutoff point with a predicted $< 10\%$ false-positive rate, and OPG-GEE examination demonstrating pressure reduction > 5.0 mm Hg. Patients who were randomized to medical management were not required to have a contrast arteriogram. Patients randomized to surgery were required to have one before surgery if they had not already had an arteriogram performed within 6 months of entering the study.[2]

Surgeon selection process. The Executive Committee recognized that a critical element for the successful conduct of this study would be the selection of highly competent surgeons to perform CEA. Competence was defined as the ability to perform CEA in asymptomatic patients with an acceptably low morbidity and mortality rate ($< 3.0\%$).

A Surgical Management Committee was formed to devise a method for selecting surgeons and to oversee the surgical conduct of the protocol (Appendix 1). The details of that deliberation have been published previously and will be briefly reviewed.[4]

As part of the initial process to determine whether a clinical center would be qualified to participate in the ACAS trial, a review of all CEAs performed at the center's affiliated hospitals during the most recent 1-year interval was required. A data sheet that provided details concerning the patient's history, the indication for surgery, whether the patient was symptomatic, the severity of carotid stenosis, and any associated complications or death was completed for each surgery. A review of these data gave the Executive Committee an overall idea of the complication rates and the number of potential cases that would be found within the center. Once the center was deemed to be qualified, each potential surgeon from that center who wished to participate was required to submit the results of his or her 50 most recent consecutive CEAs. This retrospective audit permitted the committee to examine operation date, indication for operation (asymptomatic, transient ischemic attack, stroke), duration of hospitalization, and outcome, especially with regard to whether postoperative death or stroke occurred.

The members of the Surgical Management Committee were unanimous in their opinion that both frequency of operation and outcome of a surgical sample were important parameters in judging an applicant's competence. The committee decided that 12 CEAs per year per surgeon was the minimum acceptable number. The committee also was influenced by a report from the American Heart Association that set acceptable limits for morbidity and mortality rates as a function of indication for operation.[5] Specifically, the Surgical Management Committee stated that operations performed by a given surgeon must carry a combined stroke plus

mortality rate of ≤3.0% for asymptomatic patients and ≤5.0% for all clinical indications. Only applicants whose results met these defined criteria were accepted; those whose results were inferior to the defined criteria were not approved. If an institution was unable to provide a surgeon who met the defined criteria, that institution could not be an ACAS trial center.

The Surgical Management Committee also recognized that a sample of 50 previous cases might not be sufficient to accurately reflect a surgeon's current operative morbidity and mortality rates, and for that reason the committee advised that a continuing performance audit be built into the study design. If an institution reported a postoperative complication of either death or stroke after the study commenced, that center was to be placed on a "watch" status. If a second postoperative complication occurred, an institutional audit would be triggered. This would include a re-review of both the institutional and individual surgeon's results to determine whether the individual or the entire institution should be suspended from the study because of an unacceptably high complication rate.

The cumulative data from this audit and selection process were reviewed in February 1991 before publication of the initial description of the method. One hundred sixty-four surgeons from 48 centers applied for ACAS approval. At that time, 117 applicants from 38 of the 39 ACAS centers that ultimately participated were approved. Ninety-eight of the 117 approved surgeons were general vascular surgeons and 19 were neurosurgeons. Seventeen surgeons were not approved. Thirty did not complete the application process. The basis for rejection included < 12 operations per year or an unacceptably high morbidity and mortality rate demonstrated by the review process.[4]

The 117 approved ACAS surgeons submitted 5641 CEAs for review. The average number of CEAs performed annually by each surgeon was 20. The distribution of operations as a function of clinical indication was as follows: 1511 operations (26.8%) in asymptomatic patients (mortality rate, 0.8%; stroke morbidity rate, 0.9%); 3034 (53.8%) in patients with symptoms of transient cerebral ischemia (mortality rate, 0.5%; stroke morbidity rate, 1.8%); 1096 (19.4%) in patients with a history of stroke (mortality rate, 1.6%; stroke morbidity rate, 1.9%). The overall mortality and stroke morbidity rates for all indications and all surgeons were 0.8% and 1.5%, respectively.

The Data, Safety, and Monitoring Committee was instructed by the NINDS-approved protocol to stop the study if the aggregate morbidity and mortality rate associated with CEA exceeded 3.0%. During the course of the ACAS trial, only three institutions reported a second complication resulting in an institutional review. No surgeon or institution was dropped from the ACAS trial because of an unacceptably high complication rate. During the course of the study, the Surgical Management Committee and the other participants did not know the overall operative morbidity and mortality rate, but assumed that it must be under 3.0% because the study had not been stopped. Thus the ultimate validation of the surgeon selection process awaited the completion of the study and release of the results, including the data concerning operative morbidity and mortality rates.

RESULTS

ACAS trial outcome. Between December 1987 and December 1993, 1662 patients were entered in the study and randomized to the surgical or medical treatment arm. At the time of study analysis, follow-up data were available on 1659 patients. Eight hundred thirty-four patients were randomized to best medical management, including aspirin and risk-factor control. Eight hundred twenty-five patients were randomized to CEA plus best medical management. The design of the study was intent-to-treat, and therefore the patient randomized to one arm of the study carried that study designation regardless of whether a crossover occurred.

On September 14, 1994, the study was formally stopped because the Data, Safety, and Monitoring Committee indicated a significant boundary had been crossed in favor of surgical management. The study centers and the patients who had been randomized to medical management were notified so that they could be evaluated for the opportunity to undergo surgery if they were still good surgical candidates.

The 5-year cumulative stroke risk for patients randomized to the surgical arm (including perioperative stroke and death) was 5.1%; in contrast, the 5-year stroke risk in the patients randomized to the medical treatment arm was 11%. CEA provided an absolute risk reduction of 5.9% and a relative risk reduction of 53% ($p = 0.004$).[1,2]

Analysis of surgery data. Eight hundred twenty-five patients were randomized to the surgical arm. Nineteen patients had a stroke or died within 30 days of randomization, yielding a combined stroke morbidity and mortality rate of 2.3% (95% confidence interval, 1.3% to 3.3%). Not all patients, however,

Table I. Reasons surgery was not performed

Reason	*Patient (no.)*
Refused operation	45
Ineligible for operation	
Angiogram showed stenosis <60% after randomization	27
Cardiac status contraindicated operation	12
Finding of an intracranial stenosis of greater severity	6
Stroke or death before operation	3
Miscellaneous reasons	8
Total	101

underwent surgery. In addition, not all deaths and complications occurred as a consequence of surgery. Nonetheless, in an intent-to-treat analysis all patients randomized to surgery are counted as the surgical group, and all complications occurring within the surgical group are debited against surgery.

Of the 825 patients randomized to the surgical arm, 101 did not receive CEA (Table 1). Of the 19 patients in the surgical arm who had a stroke or died, two strokes and one death occurred before surgery. Four strokes, one leading to death, occurred as complications of preoperative arteriography. Ten strokes and one fatal myocardial infarction occurred within 30 days of CEA. Therefore, of the 724 patients in whom CEA was performed, 10 had strokes within 30 days, yielding a 1.38% stroke rate; and one died within 30 days, yielding a 0.14% mortality rate, for a combined stroke morbidity and mortality rate of 1.52% (95% CI, 0.6% to 2.4%).

Three hundred ten of the 724 patients who underwent CEA had an arteriogram performed before randomization. Four hundred fourteen patients underwent arteriography after randomization but before surgery. The arteriograms were complicated by four strokes and one death from stroke after angiograms, which yielded a combined stroke morbidity and mortality rate from arteriography of 1.2%.[2]

DISCUSSION

For CEA to be an effective form of stroke prevention in asymptomatic patients, it must reduce the risk of clinically important neurologic events when compared with medical management alone. The risk of surgery in terms of neurologic complication and death must be sufficiently low as to not erase the benefit of plaque removal. Previous studies have achieved the first objective but were unable to achieve the second. For example, the first trial that compared a surgical and medical method was reported by the Joint Study of Extracranial Arterial Occlusive Disease. This study, begun in 1959, ultimately randomized 1225 patients; 621 were randomized to CEA, and 604 were treated with what was then the best medical management.

A statistically significant benefit in survival rate was seen among those treated surgically rather than those treated medically. Three hundred sixteen patients entered the study and were identified as having transient ischemic attacks without residual deficit. The incidence of subsequent transient ischemic attacks or cerebral infarction was lower in the surgical group than in the medical group. When the perioperative morbidity and mortality rate of 8% was factored in, however, the difference lost statistical significance.[6] If these trial data had been associated with the modern low risk of surgery, subsequent symptomatic trials may not have been required to establish efficacy of surgery. More recently, the Veterans Affairs trial involving asymptomatic patients was designed to compare the endpoints of transient ischemic attack, stroke, and death among patients randomized to prophylactic CEA compared with those treated with medical management alone. The outcome clearly favored CEA. When an attempt was made to evaluate the endpoint of stroke alone (which the trial was not designed to do), twice as many strokes were found in the medical group as in the surgical group. When the perioperative mortality rate was added, however, this fell just short of statistical significance.[7] In contrast, the ACAS trial, with a combined surgical neurologic morbidity and mortality rate of 1.52% of those who underwent surgery, and even with a morbidity and mortality rate of 2.3% including preoperative arteriographic and other causes of stroke and death, permitted a statistically significant benefit in favor of surgery when compared with medical management. This benefit occurred despite the relatively low event rate in the medically managed group of 2.2% per year, or 11.0% overall in 5 years.

The method described for selecting surgeons to participate in the ACAS trial appears to have been uniquely successful. The selection process for surgeons was based upon a retrospective audit of their

results for CEA. The aggregate retrospective analysis for surgeons selected to participate in ACAS documented that the surgeons had performed CEA in asymptomatic patients with a combined stroke and mortality rate of 1.7%. The ultimate validation of any method of selection, however, must depend on the surgical performance of the surgeons examined prospectively. In that analysis, the surgeons selected performed extremely well, exhibiting a combined stroke and mortality incidence of 1.52%, which was remarkably similar to the retrospective audit data.

The Surgical Management Committee made a specific point of not mandating a particular technique or series of techniques in performing CEA. The committee recognized legitimate variations for performing the operation and held that surgical results were the ultimate factor in determining which technique a surgeon chose. Therefore, these excellent results were achieved with a variety of techniques, emphasizing the fact that surgeons who perform quality work do best when they are permitted to choose the technique that they have used successfully.

Clinical application of the results of ACAS into everyday practice requires proper patient selection and careful screening of the surgeons performing this elective procedure. In ACAS it was only by requiring extensive experience with a proven track record of $< 3.0\%$ morbidity and mortality for CEA in asymptomatic patients that we were able to prove a benefit for the operation. Any deviation upward for the morbidity and mortality rates, even to the "acceptable" levels found in the Veterans Affairs Cooperative Study, would have caused ACAS to lose its significant benefit in favor of surgery. We recommend that before referring patients for asymptomatic CEA, the referring doctor should ensure that the surgeon has experience and a track record comparable with those reported in ACAS.

CONCLUSION

The technique for selecting surgeons to participate in CEA trials may serve as a model for future trials of CEA or future trials involving any other surgical method. It may also serve as a model for hospital committees evaluating surgical privileges for performance of CEA. Methods of auditing surgeons' performance have been previously published and correspond well with the outcome of the study based on prestudy surgeon selection.[8,9]

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APPENDIX I: SURGICAL MANAGEMENT COMMITTEE

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APPENDIX II. PARTICIPATING INSTITUTIONS AND ACAS-APPROVED SURGEONS IN THE ACAS STUDY*

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*After the initial review in February 1991, an additional 11 surgeons were reviewed and approved by the same process, bringing the total listing to 128. It should be noted that 103 of the 128 approved surgeons contributed to the ACAS trial.

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